



# Mortality from Acute Coronary Syndrome: Does Place of Residence Matter?

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## Abstract

**Background:** Current evidence shows inequality in the outcomes of rural and urban patients treated at their place of residence. This study compared in-hospital mortality between rural and urban patients with acute coronary syndrome (ACS) to find whether there were differences in the outcome and received treatment.

**Methods:** Between May 2007 and January 2018, patients admitted with ACS were included. The patients' demographic, clinical, and laboratory data, as well as their in-hospital medical courses, were recorded. The association between place of residence (rural/urban) and in-hospital mortality due to ACS was evaluated using logistic regression adjusted for potential confounders.

**Results:** Of 9088 recruited patients (mean age = 61.30±12.25 y; 5557 men [61.1%]), 838 were rural residents. A positive family history of coronary artery disease ( $P=0.003$ ), smoking ( $P=0.002$ ), and hyperlipidemia ( $P=0.026$ ), as well as a higher body mass index ( $P=0.013$ ), was seen more frequently in the urban patients, while the rural patients had lower education levels ( $P<0.001$ ) and higher unemployment rates ( $P=0.009$ ). In-hospital mortality occurred in 135 patients (1.5%): 10 rural (1.2%) and 125 urban (1.5%) patients ( $P=0.465$ ). The Firth regression model, used to adjust the effects of possible confounders, showed no significant difference concerning in-hospital mortality between the rural and urban patients (OR, 1.57; 95% CI, 0.376 to 7.450;  $P=0.585$ ).

**Conclusion:** This study found no significant differences in receiving proper treatment and in-hospital mortality between rural and urban patients with ACS.

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## Introduction

Disparities in health outcomes are a global public health concern as they affect a variety of population groups in

different regions. Several studies have shown a worldwide widening of rural-urban disparities in cardiovascular events.<sup>1-14</sup> Due to several plausible factors, individuals living in rural areas may experience worse cardiovascular event

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outcomes than their counterparts living in urban areas. These factors may include inferior quality of inpatient care in rural hospitals, lower likelihood of receiving lifesaving treatment, poorer access to health services, higher levels of behavioral and psychosocial risk factors, lower socioeconomic status, different clinical profiles, and lower levels of education.<sup>1-14</sup>

Unfortunately, most available studies in either developed<sup>1-6,11,12,15</sup> or developing<sup>7-10,13,14</sup> countries have compared outcomes between rural and urban patients admitted to hospitals located at their own place of residence. Such investigations often compare the facilities, competencies, and accessibilities of hospitals rather than the risk factors between rural and urban individuals. Nevertheless, owing to such factors as poverty, lower socioeconomic status, lower education levels, lesser knowledge about patients' rights, and lower demands, rural patients might be treated differently. These factors should not be assessed only by comparing rural and urban hospitals; the attainment of this goal requires that patients be admitted to the same hospital, treated by the same physicians, and medicated in similar circumstances. Therefore, the current study aimed to compare in-hospital mortality rates between rural and urban patients with acute coronary syndrome (ACS).

## Methods

Tehran Heart Center (THC), affiliated with Tehran University of Medical Sciences, is a large referral tertiary heart hospital located in the Iranian capital, Tehran. THC admits patients from all over the country. Designed based on the Patient Registry of THC, the present cross-sectional study recruited patients with first-time ACS admitted to THC between May 2007 and January 2018. Data on demographic characteristics, clinical and laboratory findings, and the in-hospital medical course were collected by trained physicians. In-hospital death was considered the endpoint of the study, and its association with place of residence (rural/urban) was assessed.

In-hospital mortality from ACS, defined as patients' death during the hospitalization course for first-time ACS, was the main dependent variable of the current study. The main independent variable was place of residence (rural/urban), defined as patients' longest stay in their place of residence (during the last 10 years). The other independent variables of this study were age, sex, family history of coronary artery disease (defined as the occurrence of premature coronary artery disease in a first-degree relative [male <45 y and female <55 y]), smoking (being a current cigarette smoker or having stopped cigarette smoking within the last month), hyperlipidemia (being on antihyperlipidemic medications, or serum total cholesterol levels  $\geq 200$  mg/dL, or serum triglyceride levels  $\geq 200$  mg/dL, or serum high-density lipoprotein cholesterol levels <35 mg/dL, or

serum low-density lipoprotein cholesterol levels  $\geq 130$  mg/dL), hypertension (being on antihypertensive drugs or blood pressure  $\geq 140/90$  mmHg), diabetes mellitus (being on antidiabetic medications, or fasting blood glucose levels  $\geq 126$  mg/dL, or 2-hour postprandial blood glucose levels  $\geq 200$  mg/dL, or blood glycosylated hemoglobin levels  $\geq 6\%$ ), body mass index (body weight divided by the square of body height), cardiac ejection fractions, serum levels of creatinine, education levels (low/illiterate  $\leq 5$  years of education vs higher >5 years of education), employment status (employed vs unemployed), and treatment recommendations. For the variable of treatment recommendations, 3 different recommendations by treating physicians (medical follow-up, percutaneous coronary intervention [PCI], and coronary artery bypass grafting [CABG]) were considered.

ACS is a range of acute myocardial ischemic states encompassing ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), and unstable angina. In the current study, patients with symptoms of cardiac ischemia associated with ST elevation on the electrocardiogram ( $\geq 0.2$  mV in leads  $V_1$ ,  $V_2$ , and  $V_3$  and  $\geq 0.1$  mV in the other leads) and a rise in cardiac enzymes (troponin or creatine kinase-myocardial band) were classified as STEMI patients. Symptomatic patients with a rise in cardiac enzymes without ST elevation were categorized as NSTEMI patients. Finally, patients with symptoms suggestive of myocardial ischemia without ST elevation and no subsequent rise in cardiac enzymes were considered unstable angina patients.<sup>16</sup>

Continuous variables are expressed as the mean and the standard deviation (SD), and categorical variables are presented as frequencies with percentages. The continuous and categorical variables-comprising demographic, laboratory, and clinical data-were compared between the rural and urban patients using the Student *t* and  $\chi^2$  tests, respectively. On the basis of the literature,<sup>11, 15, 17</sup> possible confounders such as age, sex, smoking, diabetes mellitus, hypertension, hyperlipidemia, family history of premature coronary artery disease, education levels, occupation, body mass index, ejection fractions, blood levels of creatinine, and types of treatment were included.

The association between place of residence and in-hospital mortality due to ACS was evaluated using logistic regression adjusted for potential confounders. Convergence because of rare events in the logistic regression was avoided by applying the Firth bias reduction method. Missing values were handled using imputation methods. The effects of the variables on the outcome are presented as odds ratios (ORs) with 95% confidence intervals (CIs). All the statistical analyses were conducted using IBM SPSS Statistics for Windows, version 23.0 (Armonk, NY: IBM Corp), and the "logistf" package in R software.<sup>18</sup>

The current study was conducted in accordance with the declaration of Helsinki and its subsequent modifications and

was approved by the institutional review board of THC and the Ethics Committee of the National Institute for Medical Research Development of Iran.

## Results

Between May 2007 and January 2018, a total of 9088 patients (mean age =61.30±12.25 y; 5557 men [61.1%]) were admitted to THC with a history of first-time ACS. The basic characteristics of the patients based on their place of residence are depicted in Table 1, which shows no significant differences between the rural and urban patients regarding age and sex. Concerning the cardiovascular risk factors, whereas the distribution of hypertension and diabetes mellitus between the groups did not vary significantly, a positive family history of coronary artery disease (P=0.003), smoking (P=0.002), and hyperlipidemia (P=0.026) was seen more frequently in the urban patients than in their rural counterparts. The urban patients also had a higher body mass index than the other group (P=0.013). Meanwhile, the rate of literacy was lower in the rural patients than in the urban individuals (P<0.001). Unemployment was also more

frequent among the rural participants (40.9% vs 36.3%; P=0.009).

Our data also showed higher cardiac ejection fractions in the patients residing in urban areas (47.1% vs 45.3%; P=0.003). Most of the patients were recommended to receive medical treatment (62.8%), followed by PCI (22.2%) and CABG (15.0%); nonetheless, the difference between the 2 groups was not statistically significant (P=0.153). Furthermore, during the course of hospitalization, in-hospital death occurred in 135 patients (1.5%): 10 residents of rural areas (1.2%) and 125 residents of urban areas (1.5%); the difference, however, did not constitute statistical significance (P=0.465).

To adjust for the effects of the possible confounders, we used the Firth regression model. As is shown in Table 2, after the adjustments, there was still no statistically significant difference in terms of in-hospital mortality due to ACS between the rural and urban patients (OR, 1.57; 95% CI, 0.376 to 7.450; P=0.585). Based on this model, the patients who underwent CABG had significantly higher mortality rates than those who received medical treatment (OR, 5.53; 95% CI, 1.928 to 17.482; P=0.002). Additionally, as is depicted in Table 2, the ejection fraction in the patients was

Table 1. Characteristics of the studied patients by place of residence\*

	Rural Patients (n=838)	Urban Patients (n=8250)	Total (n=9088)	P
Age (y)	61.05±11.76	61.18±12.31	61.30±12.25	0.768
Sex				0.111
Male	491 (58.6)	5066 (61.4)	5557 (61.1)	
Female	347 (41.4)	3184 (38.6)	3531 (38.9)	
FH of CAD	130 (15.9)	1628 (20.2)	1758 (19.8)	0.003
Smoking	173 (20.6)	2101 (25.5)	2274 (25.0)	0.002
Hyperlipidemia	354 (42.3)	3816 (46.3)	4170 (46.0)	0.026
Hypertension	446 (53.3)	4156 (50.4)	4602 (50.7)	0.112
Diabetes mellitus	239 (28.7)	2428 (29.5)	2667 (29.5)	0.620
Education level				<0.001
Low/Illiterate	714 (88.9)	5030 (64.1)	5744 (66.4)	
High	89 (11.1)	2814 (35.9)	2903 (33.6)	
Occupation				0.009
Employed	481 (59.1)	5134 (63.7)	5615 (63.3)	
Unemployed	333 (40.9)	2923 (36.3)	3256 (36.7)	
BMI (kg/m <sup>2</sup> )	26.97±4.60	27.41±4.66	27.33±4.65	0.013
EF (%)	45.30±14.57	47.08±12.99	47.21±13.29	0.003
Creatinine	1.19±.80	1.16±0.76	1.17±0.74	0.086
Treatment Recommendation				0.153
Medical	518 (64.3)	5004 (62.7)	5522 (62.8)	
PCI	158 (19.6)	1794 (22.5)	1952 (22.2)	
CABG	130 (16.1)	1189 (14.9)	1319 (15.0)	
In-hospital death	10 (1.2)	125 (1.5)	135 (1.5)	0.465

\*Data are presented as mean±SD, or n (%).

FH, Family history; CAD, Coronary artery disease; BMI, Body mass index; EF, Ejection fraction; PCI, Percutaneous coronary intervention; CABG, Coronary artery bypass grafting



Table 2. Adjusted effect of place of residence on in-hospital mortality

	OR	CI 95%		P
		Lower	Upper	
Urban patients	1.565	0.376	7.450	0.585
Female	0.844	0.079	7.019	0.936
Employment	1.332	0.020	14.43	0.898
Family history	1.757	0.328	6.344	0.462
Smoking	0.156	0.001	1.316	0.100
Hyperlipidemia	1.377	0.478	4.086	0.553
Diabetes mellitus	1.362	0.481	3.835	0.555
Hypertension	1.533	0.524	4.972	0.442
Recommendation				
PCI vs Medical treatment	1.882	0.330	8.135	0.437
CABG vs Medical treatment	5.532	1.928	17.482	0.002
Age	1.039	0.984	1.101	0.176
BMI	0.915	0.798	1.036	0.168
Ejection fraction	0.951	0.923	0.983	0.004
Creatinine	1.121	0.987	1.229	0.065
Education level	0.324	0.034	1.485	0.161

PCI, Percutaneous coronary intervention; CABG, Coronary artery bypass grafting, BMI, Body mass index

inversely associated with in-hospital mortality (OR, 0.95; 95% CI: 0.923 to 0.983; P=0.004).

## Discussion

The findings of the current study demonstrated no difference between rural and urban patients concerning in-hospital mortality due to ACS. Meanwhile, compared with the patients under medical treatment, those undergoing CABG had a significantly high mortality rate. Furthermore, the ejection fraction of the patients showed an inverse association with in-hospital mortality due to ACS.

The absence of difference in mortality rates between rural and urban populations, as we observed in our study, is not a global finding. Data from several studies in either developed or developing countries show that although mortality rates have consistently decreased in all socioeconomic groups globally, there is still a rural-urban inequality in this regard.<sup>1-6, 11, 14</sup> As the available literature consistently shows, the reduction in mortality rates has been greater in urban areas than in rural areas, resulting in a widening gap in the United States.<sup>19</sup> It has also been demonstrated that a rise in the level of rurality is in tandem with an increase in the all-cause mortality rate.<sup>2</sup> In Canada, similar to the United States, cardiovascular mortality is 13% higher in remote rural areas than in urban areas.<sup>20</sup> The magnitude of this disparity is even higher in Australia, where research has demonstrated a 50% higher mortality rate in rural areas than in urban areas.<sup>20</sup> Such divergent magnitudes of inequality in mortality rates between rural and urban populations have also been

reported in studies conducted in developing countries.<sup>6-10, 13, 14</sup> Meanwhile, there are some reports from England showing that cardiovascular mortality rates were higher in the urban population than in the rural population in the period between 2002 and 2004.<sup>21, 22</sup> Higher mortality rates in urban areas were also reported in studies conducted in 1950 in the United States.<sup>12</sup>

Rural and urban populations differ in several aspects such as wealth, family income, employment status, education levels, access to proper health care services, levels of available medical services, lifestyles, behaviors, body mass index, physical activity levels, risk factor profiles, health self-assessment, and transportation facilities.<sup>12, 15, 23, 24</sup> In addition, due to such reasons as different socioeconomic status, rural and urban patients may be treated differently and may be given diverse levels of treatment. These are the key differences contributing to the inequality in mortality rates between rural and urban patients. Our study, in contrast to the majority of previous studies, sought dissimilarities in treatment between rural and urban patients, which may result in findings that differ from those studies.

In our study, we found that neither the in-hospital mortality rate nor the recommended treatment by treating physicians was associated with the patients' place of residence. Coronary interventions (PCI or CABG) were distributed equally between the rural and urban patients, and we found no differences in this regard. However, comparisons of the outcomes of patients treated in different hospitals with dissimilar levels of facilities show that those treated in rural areas may suffer more. Rural hospitals, even in developed countries, may not provide lifesaving procedures such

as PCI or urgent CABG for various reasons such as the unavailability of the specialist staff and required equipment.<sup>25</sup> For patients with ACS in rural areas, revascularization is a less likely recommendation by treating physicians, who generally prefer treating their patients with medication.<sup>25</sup> Furthermore, the size of the hospital in urban areas may affect the rate of in-hospital mortality due to ACS. A recent study on 100 993 patients with ACS in Spain found that the risk-adjusted in-hospital mortality in large hospitals (>500 beds) was significantly lower than that in hospitals with fewer than 200 beds.<sup>27</sup> Moreover, treating physicians in rural areas are less likely to treat their patients according to the latest guidelines, which may somehow affect the outcomes, too.<sup>14</sup>

In the present study, the rate of smoking was considerably low among the rural patients by comparison with their urban counterparts. The prevalence of smoking in Iran is estimated at 10.6%.<sup>28</sup> The prevalence rate of cigarette smoking in our urban and rural patients was 25.5% and 20.6%, respectively. The majority of studies conducted in several countries such as the United States,<sup>11, 12, 29</sup> Australia,<sup>5</sup> Malaysia,<sup>13</sup> and Brazil<sup>30</sup> have shown higher smoking rates in their rural areas. A study from Brazil found a lower percentage of exposure to tobacco information in Brazilian villages and little relevant awareness and knowledge among rural populations, which may contribute to higher smoking rates in rural areas.<sup>31</sup>

Hyperlipidemia was another modifiable risk factor detected to be of high prevalence in the urban subjects by comparison with their rural counterparts (46.3% vs 42.3%). In contrast, some studies have reported higher prevalence rates of hyperlipidemia among rural residents.<sup>1</sup>

Another finding in our study was a higher mean body mass index among the urban patients ( $27.41 \pm 4.66$  kg/m<sup>2</sup> vs  $26.97 \pm 4.60$  kg/m<sup>2</sup>). Obesity in rural populations is nearly a worldwide finding in that it has been reported in many studies in either developed<sup>11, 12, 15, 29</sup> or developing<sup>13, 14</sup> countries. Furthermore, evidence from the United States shows that obesity prevalence in American rural areas has increased more rapidly than that in urban areas during the last 3 decades.<sup>32</sup> Additionally, there are reports from low-income areas such as India, Peru, Lima, Tamil Nadu, Benin, and Ayacucho indicating that obesity and metabolic syndrome are more prevalent in the urban populations of these countries than in their rural counterparts.<sup>33-35</sup>

Several possible factors may contribute to the higher prevalence and risk in rural populations such as insufficient awareness, unhealthy lifestyles, unsatisfactory health monitoring, poor diet, inadequate leisure physical activities, and delay in seeking health care.<sup>36</sup> That in our study we observed a low number of risk factors in the rural patients in comparison to the urban patients may indicate the efficacy of the Iranian rural health development system in providing relevant knowledge to rural people in controlling their risk factor profiles. Meanwhile, there has been an increasing trend

in unhealthy lifestyles among the urban population in terms of higher consumption of fast food, sedentary lifestyles, substandard housing, crowding, air pollution, and stress, all of which may contribute to the higher risk observed among urban patients.<sup>37, 38</sup>

The current study has some noteworthy merits. The design of our study is unique insofar as it allowed the researchers to investigate the effects of variables that could not be evaluated in previous studies. In addition, this study used a large referral tertiary hospital with nearly all the necessary facilities to treat patients with ACS. The recruitment of a large number of participants is another strong point of the present study.

Be that as it may, our study suffers from some limitations. Firstly, we were unable to collect data on the income of the patients, precluding us from determining their socioeconomic status precisely. Secondly, we evaluated only the in-hospital mortality of the patients and did not conduct a long-term follow-up to assess the effects of the independent variables of the study on the long-term outcomes of the study population. Thirdly, we considered only the in-hospital mortality of the patients and did not evaluate other major advanced cardiac events among the participants. Fourthly, we had wide CIs in consequence of cardiac events that were small in number.

## Conclusion

The present study investigated differences with respect to in-hospital mortality from ACS between urban and rural areas in Iran. After adjusting for possible confounders, we found no differences in mortality rates between the urban and rural patients. However, we recommend that further studies with long-term follow-ups of patients be undertaken to detect possible differences in the survival outcomes of ACS between the residents of rural and urban areas.

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